Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors in a large animal model

Grant Award Details

Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors in a large animal model

Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06378

Project Objective: To evaluate the engraftment and function of pluripotent stem cell-derived cardiovascular progenitors in a porcine heart injury model. The approach will be to develop methods to isolate cardiovascular progenitor (CVP) cells at different stages of differentiation, then transplant the cells and evaluate for cardiomyocyte regeneration and functional benefit, as well as for electromechanical coupling between the transplanted cells and the host.

Investigator:

Name:	Reza Ardehali
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,930,388

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors

Public Abstract: Because the regenerative capacity of adult heart is limited, any substantial cell loss as a result of a heart attack is mostly irreversible and may lead to progressive heart failure. Human pluripotent stem cells can be differentiated to heart cells, but their properties when transplanted into an injured heart remain unresolved. We propose to perform preclinical evaluation for transplantation of pluripotent stem cell-derived cardiac cells into the injured heart of an appropriate animal model. However, an important issue that has limited the progress to clinical use is their fate upon transplantation; that is whether they are capable of integrating into their new environment or they will function in isolation at their own pace. As an analogy, the performance of a symphony can go into chaos if one member plays in isolation from all surrounding cues. Therefore, it is important to determine if the transplanted cells can beat in harmony with the rest of the heart and if these cells will provide functional benefit to the injured heart. We plan to isolate cardiac cells derived from human pluripotent stem cells, transplant them into the model's injured heart, determine if they result in improvement of the heart function, and perform detailed electrophysiology studies to determine their integration into the host tissue. The success of the proposed project will set the platform for future clinical trails of stem cell therapy for heart disease.

Statement of Benefit to California: Heart disease remains the leading cause of mortality and morbidity in the US with an estimated annual cost of over $300 billion. In California alone, more than 70,000 people die every year from cardiovascular diseases. Despite major advancement in treatments for patients with heart failure, which is mainly due to cellular loss upon myocardial injury, the mortality rate remains high. Human embryonic stem cells (hESC) and induced pluripotent stem cells (iPSC) could provide an attractive therapeutic option to treat patients with damaged heart. We propose to isolate heart cells from hESCs and transplant them in an injured animal model's heart and study their fate. In the process, we will develop reagents that can be highly valuable for future research and clinical studies. The reagents generated in these studies can be patented forming an intellectual property portfolio shared by the state and the institution where the research is carried out. Most importantly, the research that is proposed in this application could lead to future stem cell-based therapies that would restore heart function after a heart attack. We expect that California hospitals and health care entities will be first in line for trials and therapies. Thus, California will benefit economically and it will help advance novel medical care.